

**What is Claimed Is:**

1. A method for genetically transforming an avian cell, comprising:  
delivering to an avian cell having a first recombination site a nucleic  
acid molecule comprising a second recombination site;  
5 delivering a source of integrase activity to the avian cell; and  
maintaining the avian cell under conditions suitable for the integrase to  
mediate recombination between the first and the second recombination  
sites, thereby integrating the nucleic acid molecule into the nuclear  
genome of the avian cell.  
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2. The method of Claim 1, wherein the avian cell is selected from the group  
consisting of a stage I cell, a stage X blastodermal cell, a primordial germline  
cell and an oviduct cell.
- 15 3. The method of Claim 1, wherein the integrase is a serine recombinase
4. The method of Claim 1, wherein the integrase is the bacteriophage phiC31  
integrase.
- 20 5. The method of Claim 1, wherein the source of integrase activity is delivered to  
the avian cell as a polypeptide.
6. The method of Claim 1, wherein the source of integrase activity is expressed  
from a polynucleotide molecule delivered to the avian cell.  
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7. The method of Claim 6, wherein the polynucleotide molecule is an mRNA.
8. The method of Claim 6, wherein the polynucleotide molecule is an expression  
vector.  
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9. The method of Claim 8, wherein the expression vector comprises a promoter operably linked to a region encoding the integrase, wherein the promoter is selected from a CMV promoter and an RSV promoter.
- 5 10. The method of Claim 9, wherein the expression vector comprises a nucleotide sequence selected from SEQ ID NOs: 1 and 9.
11. The method of Claim 1, wherein the nucleic acid molecule comprises an isolated gene expression control region operably linked to a region encoding a polypeptide selected to be expressed by an avian cell.
- 10 12. The method of Claim 1, wherein the nucleic acid molecule is an expression vector.
- 15 13. The method of Claim 12, wherein the expression vector is selected from the group consisting of a plasmid, an artificial chromosome, an isolated eukaryotic chromosome, an adenovirus vector and a lentivirus vector.
14. The method of Claim 11, wherein the gene expression control region is isolated from an avian gene selected from the group consisting of an ovalbumin gene, a lysozyme gene and an ovomucoid gene.
- 20 15. The method of Claim 11, wherein the nucleic acid molecule further comprises an IRES operably linked to a region encoding a second polypeptide selected to be expressed by an avian cell.
- 25 16. The method of Claim 11, wherein the region encoding the polypeptide is codon-optimized for expression of the polypeptide by the avian cell.
- 30 17. The method of Claim 15 wherein the region encoding the second polypeptide is codon-optimized for expression of the polypeptide by the avian cell.

18. The method of Claim 1, wherein the first recombination site is a attP site having at least 25% identity to the sequence according to SEQ ID NO: 11.
- 5 19. The method of Claim 1, wherein the first recombination site is a attP site having at least 75% identity to the sequence according to SEQ ID NO: 11.
20. The method of Claim 1, wherein the first recombination site is a attP site according to SEQ ID NO: 11.
- 10 21. The method of Claim 1, wherein the first recombination site is a pseudo-attP site.
22. The method of Claim 1, wherein the nucleic acid molecule and the source of integrase activity are sequentially delivered to the isolated avian cell.
- 15 23. The method of Claim 1, wherein the nucleic acid molecule and the source of integrase activity are concurrently delivered to the isolated avian cell.
- 20 24. The method of Claim 1, wherein the avian cell is a chicken cell.
25. The method of Claim 1, wherein the avian cell is a quail cell.
26. The method of Claim 1, wherein the nucleic acid molecule and the source of integrase activity are delivered to the avian cell by a method or combination of methods selected from injection, electroporation, DNA-PEI, virus-PEI, microcell fusion, artificial viral coats, polylysine conjugation and lipofection.
- 25 27. The method of Claim 1, wherein the avian cell is an oviduct cell in the oviduct of an avian and further comprising the steps of:
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before delivering the nucleic acid molecule and source of integrase activity, surgically exposing the luminal surface of the oviduct of an avian;  
delivering the nucleic acid molecule and the source of integrase activity to the oviduct cell by depositing the nucleic acid molecule and the source of integrase activity on the luminal surface;  
applying an electroporation pulse across the wall of the oviduct, wherein the electroporation pulse is directed to deliver the nucleic acid molecule and the source of integrase activity to recipient oviduct cells, whereby the integrase mediates integration of the nucleic acid molecule into the genome of a recipient cell;  
surgically closing the oviduct; and  
maintaining the avian under conditions suitable for the expression by the recipient oviduct cells of a polypeptide encoded by the nucleic acid molecule and deposition of said polypeptide into the white of a laid hard shell egg.

28. A genetically transformed avian cell, and progeny thereof, generated by a of the methods according to Claims 1.
29. A genetically transformed avian, and progeny thereof, generated by the method according to Claim 27.
30. A method for generating a genetically transformed avian, comprising:  
genetically transforming an avian cell by a method according to Claim 1;  
delivering the genetically transformed avian cell to an early stage avian embryo, thereby generating a genetically transformed embryo;  
and  
maintaining the avian embryo under conditions suitable for the embryo to develop and hatch as a transgenic chick.

31. The method of Claim 26, wherein the genetically transformed embryo is delivered to a recipient female avian and laid as a hard shell egg.
- 5 32. A method of producing a polypeptide comprising expressing the polypeptide in a transgenic avian cell, said cell comprising a heterologous nucleic acid molecule that expresses the polypeptide, wherein the heterologous nucleic acid molecule is integrated into the nuclear genome and flanked by halves of an integration site recognized by an integrase.
- 10 33. A polypeptide of interest expressed by a genetically transformed avian cell, and progeny thereof, the cell comprising a heterologous nucleic acid molecule integrated into the nuclear genome thereof by an integrase, and wherein the nucleic acid molecule comprises a region encoding the polypeptide of interest and an operably linked promoter region.
- 15 34. The polypeptide according to Claim 33, wherein the polypeptide is an immunoglobulin chain.
- 20 35. The polypeptide according to Claim 33, wherein the polypeptide is a cytokine.
36. The polypeptide according to Claim 33, wherein the polypeptide is deposited in the white of an avian egg.
- 25 37. The polypeptide according to Claim 33, wherein the polypeptide is expressed by a transgenic bird comprising the genetically transformed avian cell.
38. The polypeptide according to Claim 37, wherein the genetically transformed avian cell, and the progeny thereof, are generated according to the methods of Claim 1.
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39. The polypeptide according to Claim 37, wherein the transgenic bird is generated according to the method of Claim 30.
40. An avian egg white comprising a heterologous polypeptide produced according to the method according to the Claim 32.
41. An avian egg comprising a heterologous polypeptide produced according to the method according to the Claim 32.
42. A method for generating a genetically modified avian cell, and progeny thereof, using a tagged chromosome, said method comprising the steps of:  
providing an isolated modified chromosome comprising a lac operator region and a first recombination site;  
delivering the modified chromosome to a avian cell, thereby generating a trisomic avian cell;  
delivering to the avian cell a source of a tagged polypeptide comprising a fluorescent domain and a lac repressor domain;  
delivering a source of integrase activity to the avian cell;  
delivering a polynucleotide comprising a second recombination site and a region encoding a polypeptide to the avian cell;  
maintaining the avian cell under conditions suitable for the integrase to mediate recombination between the first and second recombination sites, thereby integrating the polynucleotide into the modified chromosome and generating a genetically modified avian cell;  
expressing the tag polypeptide by the avian cell;  
allowing the tag polypeptide to bind to the modified chromosome so as to label the modified chromosome; and  
isolating the modified chromosome by selecting modified chromosomes having a tag polypeptide bound thereto.

43. The method according to Claim 42, further comprising the step of delivering the modified chromosome to a second avian cell to generate a trisomic avian cell.
44. A modified avian chromosome comprising a lac operator region and a recombination site.
45. The avian chromosome according to Claim 44, wherein the lac operator region is a concatamer of lac operators.
46. The avian chromosome according to Claim 44, wherein the recombination site is selected from an att B or an att P site.
47. The avian chromosome according to Claim 44, further comprising a region encoding a tag polypeptide and an operably linked promoter.
48. The avian chromosome according to Claim 47, wherein the tag polypeptide comprises a fluorescent domain and a lac repressor domain.
49. The avian chromosome according to Claim 44, wherein the fluorescent domain is GFP.
50. The avian chromosome according to Claim 45, further comprising a heterologous polynucleotide integrated into the first recombination site.
51. The avian chromosome according to Claim 50, wherein the heterologous polynucleotide comprises a region encoding a polypeptide operably linked to a promoter.
52. The avian chromosome according to Claim 50, wherein the promoter is an avian promoter selected from the gene expression control region of an onomucoid gene, a lysozyme gene and an ovalbumin gene.